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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,894	03/09/2004	Joachim Brendel	DEAV2003/0023 US NP	2872
5487	7590	12/21/2007		
ANDREA Q. RYAN SANOFI-AVENTIS U.S. LLC 1041 ROUTE 202-206 MAIL CODE: D303A BRIDGEWATER, NJ 08807			EXAMINER PACKARD, BENJAMIN J	
			ART UNIT 4173	PAPER NUMBER
			NOTIFICATION DATE 12/21/2007	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/796,894	Applicant(s) BRENDAL ET AL.	
	Examiner Benjamin Packard	Art Unit 4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) 8-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date (<u>4 sheets</u>). | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-7, drawn to compositions) in the reply filed on 11/15/2007 is acknowledged. The restriction is made final.

Claims 8-12 are rejected as being directed towards the non-elected group.

Applicants also elected the following species: ibutilide as the IKr channel blocker and the compound of Example 1, 2'-[[2-(4-methoxyphenyl)acetylamino]methyl]biphenyl-2-carboxylic acid (2-pyridin-3-ylethyl)amide as a species of formula Ib.

Claim Rejections - 35 USC § 112

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapy of atrial fibrillation or atrial flutters, does not reasonably provide enablement for prophylaxis of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation, See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) cited at MPEP 2164.01(c).

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is

Art Unit: 1614

meant by “undue experimentation,” the Federal Circuit has stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).¹

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, all Wands factors have been considered and the following factors that are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level

The invention relates to drug compositions. The relative skill of those in the art is high, that of an MD or PHD. That factor is outweighed, however, by the unpredictable nature of the art. As illustrative of the state of the art, the examiner cites Lee et al., Atrial flutter: A review of its history, mechanisms, clinical features, and current therapy, Current Problems in Cardiology, Volume 30, Issue 3, pages 121-167. See page 149 which discusses the difficulty of suppressing arrhythmia.

2. The breadth of the claims

Since the instant specification provides no limiting definition of the term “prophylaxis”, the examiner will adopt the broadest reasonable interpretation for same. Webster’s Online Dictionary defines “prophylaxis” as “prevent the spread of disease” and prevent is defined as “to keep from happening or existing”, i.e., to completely eradicate.

The claims are thus very broad insofar as they recite the “prevention” of atrial fibrillation or atrial flutters, i.e., the complete eradication of same. While such “prevention” might theoretically be possible under strictly controlled laboratory conditions, as a practical matter it is nearly impossible to achieve in the “real world” in which patients live; atrial fibrillation or atrial flutters is always a risk.

3. The amount of direction or guidance provided and the presence or absence of working examples

¹ As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is “undue”, not “experimentation”.

The specification provides no direction or guidance for the prevention of atrial fibrillation or atrial flutters. No reasonably specific guidance is provided concerning useful therapeutic protocols for preventing atrial fibrillation or atrial flutters.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed agents could be predictably used to prevent atrial fibrillation or atrial flutters as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

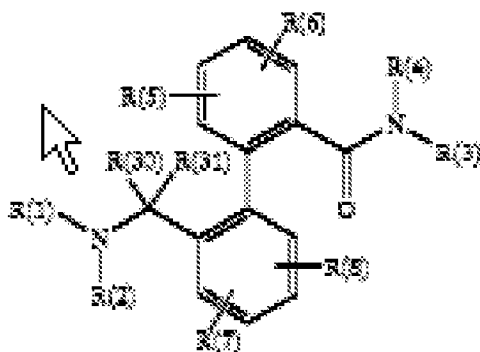
1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

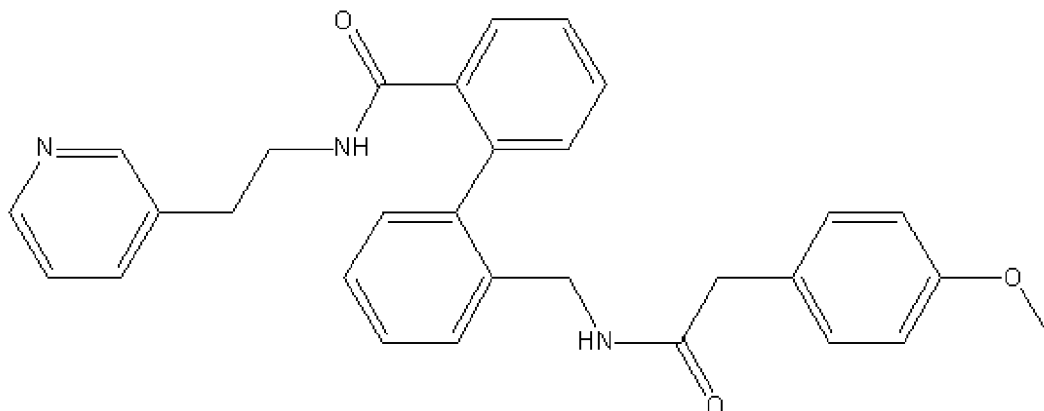
Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brendel et al (US 6,531,495, '495, filed Oct 30, 2000, granted 3/11/2003), in view of Smith et al (US Pregrant Pub 2002/0161018).

'495 teaches in claims 1 and 15 the composition comprising a compound of structure:



(see example 4i columns 45-46) , which is

the elected specie as shown:



2'-[[2-(4-methoxyphenyl)acetyl]amino]methyl]biphenyl-2-carboxylic acid (2-pyridin-3-ylethyl)amide

and an effective amount of an IKr channel blocker (see claim 15). '495 does not teach ibutilide as the specific IKr channel blocker or administration sequences.

Smith et al teaches the IKr channel blocker, Ibutilide. At paragraph 25, teaches "ibutilide ... may enhance the potency of local anesthetics by blocking the IKr channel," thereby placing ibutilide in the category of IKr channel blockers.

Therefore, one of ordinary skill in the art would recognize that when making a composition according to '495, it would be obvious to use a known IKr channel blocker, such as taught in Smith et al where an IKr channel blocker is called for. Additionally, any sequencing of the composition administration is obvious where claim 7 is directed to all possible sequences, i.e. simultaneous, separate, and sequential.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN PACKARD whose telephone number is (571)270-3440. The examiner can normally be reached on M-R 9-4:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

11 December 2007
BP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614